HISTORICAL ARCHIVES

The Use of Copper, Cobalt, Manganese, and Iodine in the Treatment of Undulant Fever

By Francis M. Pottenger Jr.

Summary: One of the great original thinkers of his day, Dr. Francis M. Pottenger Jr. devoted his career to the prevention of chronic illness and made lasting contributions in the field of nutrition science, particularly in his classic book *Pottenger's Cats*. In this deeply researched article, Dr. Pottenger presents years of scientific literature documenting the impact of nutrient-deficient soil on human health.

In 1951, one year after the publication of this article, Standard Process introduced Trace Minerals-B12 (formerly known as Allorganic Trace Minerals B12), largely based on the research presented here. Trace Minerals-B12 contains some of the important trace minerals discussed below—namely iodine, zinc, copper, and manganese—in order to support enzymatic reactions in the body.

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The Use of Copper, Cobalt, Manganese, and Iodine in the Treatment of Undulant Fever

—Reprinted from *The Transactions of the American Therapeutic Society,* Volumes XLVIII and XLIX, 1950.

Preliminary report: Scientific literature on soil deficiency and medical literature on the effect of soil deficiencies on human health are presenting an increasingly interrelated picture. Reports of the roles played by certain trace elements in domestic animals led to the use of these elements in the treatment of undulant fever. A review of significant literature and our therapeutic results with a mixture of cobalt, manganese, copper and iodine are presented in the hope that other physicians will undertake further study of these minerals.

Wilgus, Norris, and Heuser[1] showed that lack of manganese is responsible for slipped tendon disease in chickens. In animals, a close relationship between manganese and the development and size of bone was demonstrated by Amdur, Norris, and Heuser,[2] while Fairbanks and Krider[3] stressed the necessity of manganese in the prevention of rickets.

In discussing the relationship of manganese to cobalt polycythemia, Orten and associates[4] emphasized the importance of this element in iron assimilation. Wachtel, Elvehjem, and Hart[5] presented further evidence of the role of manganese in iron assimilation, as did Perla, Sandberg, and Holly[6] in their discussion of the interdependence of manganese and the assimilation of vitamin B.

Perla and Sandberg[7] also showed that manganese will neutralize the toxic effects of vitamin B. Harmer and Sherman[8] reported on the influence of manganese in the synthesis of vitamin C in the foliage of plants. An interesting study by Orent and McCollum[9] indicated that manganese deprivation results in sterility of male and female animals and also in lack of maternal instinct. Perla and Marmorston[10] reviewed the effect of manganese on natural resistance to disease. Walbum and Morch[11] reported that the chloride of manganese enhances resistance to tubercle bacilli, increases the production of diphtheria antitoxin and augments the titer of Bacillus coli sera.

Hart, Steenbock, Waddell, and Elvehjem[12] stressed the importance of the essential nature of copper in the formation of blood. Keil, Keil and Nelson[13] and Keil and Nelson[14] reported the effects of this element on the pigmentation of the skin.

Cobalt has long been recognized as essential in animal nutrition. The tremendous loss of sheep in Australia and New Zealand was shown by Wunsh[15] and Underwood and Filmer[16] to be caused by insufficient amounts of cobalt in the soil producing forage consumed by the animals.

The investigations carried on at the Cawthron Institute at Nelson, New Zealand, by a large group of scientists[17a–n] constitute a monumental study on trace element deficiency.

Abbott and Ahmann[18] observed a general condition of malnutrition among people living on farms in Florida where copper and other trace elements are known to be deficient. Orten and associates,[19] and Stare and Elvehjem[20] showed the relationship of cobalt to polycythemia. Askew[17d] emphasized the importance of cobalt in breeding ewes.

Marine and his coworkers[21,22] demonstrated that a small amount of iodine is essential to the prevention of goiter. Harington[23] showed that iodine is necessary in the production of thyroxin. Curtis and Phillips[24] stated that feeding of large amounts of iodine to cattle increases the milk production of these animals, raises the butterfat content, and diminishes sterility. Potassium iodide has long been used in the treatment of arteriosclerosis. Levis and Emery[25] and Levis[26] observed spectroscopically that a constant relationship appeared to exist between subnormal amounts of copper, cobalt, and manganese in the tissues of cattle and the presence of Bang's disease [aka brucellosis]. They showed that the blood and brains of animals slaughtered because of this disease revealed an extreme deficiency of these elements. Erf[27] taught that a relationship exists between the presence of Bang's disease and lack of iodine, copper, cobalt, and manganese; during the years from 1938 to 1942, he treated cattle suffering from Bang's disease with a drench of these salts, with the result that some positive agglutinations reverted to negative. Levis[26] showed spectroscopically that the brain of Bang reactor cows contained only about one-tenth of the amount of manganese found in normal animals; that no cobalt was present and that copper was depleted.

That copper deficiency produces enzootic ataxia in sheep found in many parts of the world was suggested by Stewart[28] and Bennetts.[29] Copper was shown to prevent the effect of molybdenum poisoning from teart soils by Ferguson, Lewis, and Watson.[30]

I became interested in the possibility that lack of manganese, copper, cobalt, and iodine might have some bearing on pigmentation shown by a number of my patients suffering from low energy states.[31] These symptoms were attributed to a disturbance in fat metabolism. The patients showed bronzing of the hair and dark pigmentation about the eyes, areola of the nipples, midline of the abdomen, anus, and genitals. In some instances, a general bronzing or salmon-colored cast to the entire body was noted. Extreme pallor of the conjunctiva was common. A purplishness of the buccal membranes was often found. Anemia, usually excessive nasal and ocular discharge, bronchitis, and frequently diarrhea were also seen. Sterility was common.

Recognizing that certain of the phosphatases and other fat-splitting enzymes are activated[32] by the addition of small amounts of manganese, iron, and cobalt and, as shown by Curtis and Phillips,[24] and that iodine is important in fat metabolism, I began to use a mixture of these salts in the treatment of patients who showed hyperpigmentation. A mineral salt mixture was compounded, consisting of the following:

Manganous sulfate	1	**H2O**	50.00g
Copper sulfate	5	**H2O**	5.00g
Cobaltous sulfate	7	**H2O**	.25g
Potassium iodide			.50g

Compound into a solution with distilled water to make eight ounces. Do not compound into a syrup. This material may also be made into 60 or 120 capsules and must be kept dry.

This mixture was divided into from 60 to 120 doses. Occasionally in sensitive individuals the dose may be dropped to 10m and gradually returned to the full dose. One dose was administered at each meal on a full stomach. The dosage of each salt was well within the range of tolerance of the individuals, as described by Sollman,[33] and each salt was tested separately. We found that manganese given alone appeared to offer some help but was not constant in its action. Cobalt, likewise, offered some suggestive assistance. Iodine given alone apparently had no profound effect nor did copper in the form of sulfate. However, the combination of these four metals as manganous sulfate, cobaltous sulfate, potassium iodide, and copper sulfate had desirable effects. Increase in the energy level of the patients was noted before any change of pigmentation was apparent. The emerging hair was the first place to show a loss of the generalized bronzing. Inasmuch as these salts were slightly irritating to the gastric mucosa, the dose was given on a full stomach. Copper apparently inhibits certain of the enzymes of starch metabolism, as was demonstrated by Sumner and Somers[34] and von Euler and Svanberg.[35] We found that it interferes with carbohydrate digestion and, likewise, that the cuprous ion is much more powerful in the inhibition of starch utilization than is the cupric. Therefore, the intake of carbohydrates in highly refined form, such as sugars and starches, must be reduced to a minimum when copper is used in medication. In spite of the fact that copper seems to interfere with other enzyme systems[36] that manganese and cobalt activate, there is some synergistic effect that is desirable.

The results obtained by Erf[27] in the treatment of Bang's disease in cattle suggested the possibility of using this mineral salt mixture in the treatment of two of my patients with undulant fever.

Schreiner[37] reported five cases of undulant fever that he treated with radioactive colloidal manganese in 1943. All five patients showed marked improvement, although the results of succeeding agglutination tests were not reported.

The difficulty of making a positive diagnosis of brucellosis is well known. Although Meyer and Fleischner[38] reported nearly 100 percent positive correlation of the skin test in infected guinea rigs, Levin[39] asserted that this test is inconstant in human beings. According to Borts,[40] the test for brucellosis must be interpreted in a manner similar to the tuberculin test. He further stated that agglutination tests must be performed begore skin tests are made in order to avoid false transient low titers.

Case Reports

Case 1. — The patient, a male dentist 37 years of age, gave a history of periodic stomach upsets, vomiting, general malaise, loss of appetite and hyperpigmentation about the eyes. For a period of 10 years he had suffered from vague abdominal pains, joint pains, and chest pains. He frequently ran a temperature of 99.5°F, with chills. He was subject to attacks of dizziness, exhaustion, and extreme irritability, followed by depression. He had previously been examined for tuberculosis and other diseases without positive diagnosis.

Physical examination revealed the following salient findings: Rough, dry skin with hyperpigmentation about the eyes and mouth, under the arms and about the umbilicus and genitals; grating in the shoulders and knees with a suggestion of some fluid in both knees; a few shotty glands in both inguinal areas and the axillae as well as the femoral canals; liver slightly enlarged; splenic dullness materially increased; potential inguinal hernia on the right.

In January 1945 the patient showed an agglutination of over 1:2560, positive for brucellosis. A mineral salt mix cure of manganese, cobalt, copper, and iodine was prescribed. The ratio of the salts was manganese 500, copper 50, cobalt 2.5, and iodine 5.

Subsequent agglutination tests were made by a laboratory near the patient's home and the records were lost. On February 8, 1945, our laboratory again made an agglutination test, the results of which had dropped to 1:1280. At this time the patient's skin was regaining the normal pink color and he reported that his energy level was rapidly rising. By May 1945 he declared that he had more energy than he had had for years. The result of his agglutination test had become negative and, aside from an occasional dull headache, he considered himself in excellent health. In May 1947 the agglutination reaction was still negative, and he reported that, with the exception of symptoms from a slowly emptying gallbladder, he had enjoyed good health.

Case 2. — The patient, a 48-year-old female teacher, gave a history of headaches, lack of energy, periods of extreme exhaustion and intractable insomnia for about a year. In 1930 she had experienced an attack of severe weakness and vertigo, lasting about a week and accompanied by severe gastric distress. Similar attacks, with heavy head colds, had occurred since that time, and she was acutely sensitive to noise.

Physical examination in 1943 revealed a marked pigmentation about the eyes, folds of the arms and breasts; generalized bronzing over the body; many areas of ecchymosis over the body; spongy gums; linear scar of keloid formation on the left breast; enlargement of the lower thoracic lymph nodes; spleen about three times normal size; abdominal reflexes lacking; results of spinal fluid examination essentially negative.

Over a one-year period of observation, the patient frequently complained of vague muscular pains and poor coordination.

In 1944 the patient enrolled as a graduate student at a middle western college. During the first weeks of school she ran a high temperature with an influenza-like episode. She also had a blister on her heel. Five days of observation in the hospital revealed no definite cause of the fever. She did not complain of gastrointestinal symptoms at this time. Upon her return to school she was weak and unable to follow directions. She again ran a temperature of 103°F and a second episode of fever occurred 10 days later. All of these episodes were accompanied by chills and profuse perspiration. No further attacks of fever were noted during the remainder of the school year.

In late December 1944, tenosynovitis developed about the extensor tendon of the left thumb, and the patient was incapacitated for several months. She also reported pain in the left hip and showed an extremely low energy level.

When the patient called at my office in August 1945, she complained of incoordination and pain in the left wrist. Examination revealed a positive Babinski reflex on the right with hyperactive knee reflexes. Undulant fever was suspected; results of agglutination tests were positive (1:20 and 1:40). Blood culture yielded negative results.

A mixture of cobalt, copper, manganese, and iodine was prescribed at this time and was taken regularly for one year. In October 1945 the agglutination reaction was negative. The patient had become relatively free from symptoms except under conditions of extreme fatigue. In May 1947 the agglutination reaction was still negative. No return of pain in the joints was reported, and the patient is now in relatively good health.

Case 3. — The patient, a boy nine-and-a-half years of age, was first seen by us in March 1947. His previous physician reported a history of constant sleepiness and a temperature up to 100°F over a 14-week period. Intracutaneous tests had been positive for brucellosis, and agglutination tests were reputed to be positive, although we were unable to obtain the laboratory reports.

Our examination revealed a boy with marked bronzing over the entire body, particularly over the genitals and about the paps as well as the terminal phalanges of the fingers; considerable grating in the ankles and knees, wrists and elbows; skin extremely dry; some crowding of the teeth; slight harshness of breath sounds; impure mitral sound of the heart, and slight reduplication of the pulmonic sound; blood pressure 120 systolic and 70 diastolic; some glands in the posterior triangle of the neck. Results of an agglutination test were negative.

After a thorough study and because of the history of continued low energy, bouts of fever, and pigmentation, we prescribed a mineral salt mixture in March 1947. In May 1947 the patient's agglutination was still negative. On subsequent visits he showed a lessening of the bronzing, and his mother reported that he was regaining his energy and spontaneousness as well as showing considerable gain in his school work.

Case 4. — The patient, a 38-year-old male dentist, gave a history of low energy, frequent night sweats, clammy hands and feet, considerable dizziness, tinnitus and loss of memory, intermittent diarrhea and constipation over a two-year period. He had been rejected by the Army with a diagnosis of brucellosis.

Physical examination revealed marked bronzing of the phalanges of the fingers and toes, salmon-colored cast to the entire body; marked bronzing about the orbits, paps, genitals and rectum; splenic dullness materially increased; size of the liver slightly increased; genitals very large. The blood pressure at the time of the first examination was 102 systolic and 64 diastolic.

In August 1945 a mixture of manganese, cobalt, copper, and iodine was prescribed, and the dose was doubled a few weeks later. By October 1945 the pigmentation was beginning to lessen and the patient reported an improved energy level. His blood pressure had also improved, rising to 120 systolic and 80 diastolic. In December he reported that he no longer suffered from night sweats and that the excessive daytime perspiration had diminished. By February 1946 he reported complete freedom from night sweats, continued lessening of pigmentation, and the return of the genitals to normal size. In April 1946 he had one night sweat and suffered a short period of lowered energy. He resisted respiratory infections during periods when other members of his family contracted them. Some gastric distress developed, at which time we cut the dose of mineral salts in half. The patient has come to the office at regular intervals and has continued to report greater energy than in years. At present he is taking the mineral salt mixture only during occasional periods of depressed energy

Summary

Levis[26] showed that the amounts of cobalt, manganese, and copper are deficient in the nervous tissues and blood of cattle afflicted with Bang's disease. Erf[27] obtained a reversion of agglutination from positive to negative in cattle by using a drench of manganese, cobalt, copper, and iodine, and suggested that brucellosis is attended by a deficiency of these elements. Schreiner[37] described five patients with undulant fever who improved under treatment by radioactive colloidal manganese.

A mineral salt mixture containing cobalt, manganese, copper, and iodine was used by the author in the treatment of four patients with low energy who showed hyperpigmentation. Of these patients, two were apparently suffering from brucellosis. The remaining two presented suggestive symptoms that had previously been diagnosed as brucellosis by other physicians; however, records of previous positive agglutinations could not be found. The results of treatment in all four patients were encouraging.

This study is presented in the hope that other physicians who have patients in whom the diagnosis of brucellosis has definitely been established will further explore the therapeutic possibilities of these minerals.

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‹ Applied Trophology, Vol. 8, No. 10 (October 1964)

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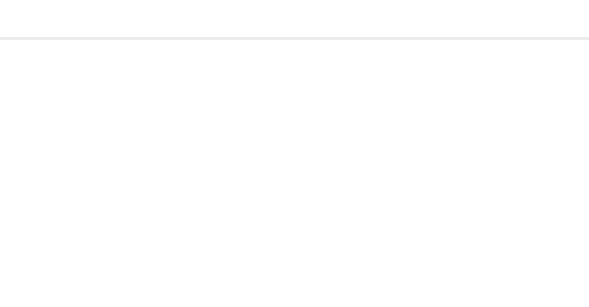

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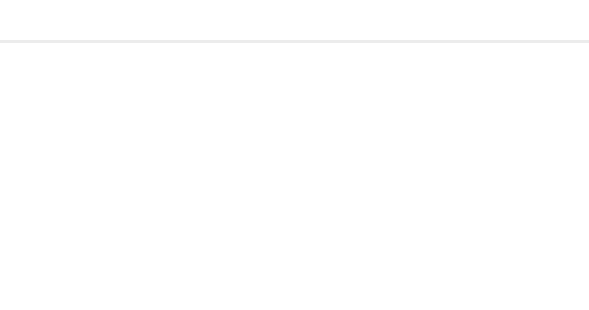

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